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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/676,734	09/29/2000	Charles Joel Amtzen	P00245US D	1914

7590 03/17/2004

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EXAMINER

COLLINS, CYNTHIA E

ART UNIT PAPER NUMBER

1638

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/676,734

**Applicant(s)**

ARNTZEN ET AL.

**Examiner**

Cynthia Collins

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 73-75,83,84 and 98-101 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 73-75,83,84 and 98-101 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)          |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. <u>15</u> .  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____.  | 6) <input type="checkbox"/> Other: _____.                                   |

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### **DETAILED ACTION**

The amendment filed on December 18, 2003 has been entered.

Claims 73, 83, 84, 98, 99 and 100 are currently amended.

Claims 1-72, 76-82 and 85-97 are cancelled.

Claim 101 is newly added.

Claims 73-75, 83-84 and 98-101 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

### ***Claim Rejections - 35 USC § 112***

Claim 84 remains rejected, and claims 73-75, 83 and 98-101 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the transgenic plants expressing the specific animal viral antigens at the levels set forth in Applicant's working examples, does not reasonably provide enablement for expressing in all plants recombinant viral antigen proteins obtained from all animal viruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed August 13, 2003.

Applicants' arguments filed December 18, 2003, have been fully considered but they are not persuasive.

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Applicant points to the amendment of claim 84 to recite the specific expression level exemplified. With respect to claim 83, Applicant submits that the specification is enabling for achieving the levels of expression necessary to elicit an immune response in an animal upon consumption of the claimed transgenic plants. With respect to claim 98, Applicant submits that the specification is enabling for proteins from sources other than the exemplified recombinant transmissible gastroenteritis virus (TGEV) S-protein and recombinant hepatitis B surface antigen (HbsAg) protein, as the specification discloses in detail the identity of other specific antigens that may be useful for practicing the claimed invention (reply pages 5-6).

The rejection is maintained because the specification is not enabling for expressing at the claimed levels in all plants recombinant viral antigen proteins obtained from all animal viruses, since the level of expression of different recombinant proteins in transgenic plants is affected by multiple variables and is thus unpredictable, as discussed at pages 5-6 of the office action mailed August 13, 2003. See, for example Sanders et al. (Nucleic Acids Research, 1987, Vol. 15, No. 4, pages 1543-1558), who teach transgenic plants comprising an NPTII transgene, where NPTII transcripts were 30-fold higher, and NPTII enzyme activity was 110-fold higher, when the NPTII transgene was operably linked to a CaMV 35S promoter and leader sequence as compared to a nopaline synthase promoter and leader sequence (page 1543 abstract; page 1553, Table 1). See also, for example, Gallie (Annual Review of Plant Physiology and Plant Molecular Biology, 1993, Vol. 44, pages 77-105), who teaches that mRNA elements such as the cap, leader sequence, initiation codon context, codon usage, stop codon and polyadenylation can affect the level of gene expression in plants (pages 77-87). See additionally, for example, Viestra, (Annual Review of Plant Physiology and Plant Molecular Biology, 1993, Vol. 44, pages 385-410), who

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teaches that protein stability is a factor to be considered when attempting to express recombinant proteins in transgenic plants, as plant cells can recognize and degrade foreign proteins (page 389 second paragraph). The expression of only two different recombinant animal viral antigen proteins at the desired levels in transgenic plants as exemplified in the instant application does not provide sufficient guidance with respect to how one may express a multitude of structurally and functionally distinct animal viral antigen proteins at the desired levels. Likewise, the recitation in the specification of a multitude of known animal viral antigen proteins does not provide sufficient guidance with respect to how one may express these structurally and functionally distinct animal viral antigen proteins at the desired levels in transgenic plants.

Claim 100 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the office action mailed August 13, 2003.

Applicants' arguments filed December 18, 2003, have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn in light of the amendment of claim 100, which removes the language at issue (reply page 7).

While the amendment of claim 100 addresses all but one of the issues previously raised under 35 U.S.C. 112, second paragraph, the rejection is maintained because it is still unclear where or in what context the mucosal immune response occurs, as the claim recites no context or location.

***Claim Rejections - 35 USC § 102***

Claims 73-75 and 98-100 remain rejected, and claims 83-84 and 101 are rejected, under 35 U.S.C. 102(e) as being anticipated by Goodman et al. (U.S. Patent 4,956,282, issued September 11, 1990), for the reasons of record set forth in the office action mailed August 13, 2003.

Applicants' arguments filed December 18, 2003, have been fully considered but they are not persuasive.

Applicant points out that the currently amended independent claims encompass features not present or contemplated by Goodman. Applicant additionally points out that where Goodman discloses the production primarily of digestive enzymes, and notes but does not exemplify that they retain physiologic activity when purified, the instant invention does not necessarily require that the protein retain physiologic activity, but rather requires that the protein structure be maintained long enough to elicit an immune response. Applicant further points out that it was not known in the art at the time of the Goodman reference whether an antigen expressed in a plant consumed by an animal would be digested or be presented to the immune system to allow for recognition, as illustrated by the submitted reference of Service (Science, 1994, Vol. 263, pages 1522-1524). Applicant also asserts that the levels of expression disclosed in Goodman would not be high enough to achieve an immune response. Applicant additionally points out that Applicant's work is peer recognized as the first actual incident of the production of immunogenic viral proteins in plants, as illustrated by the submitted reference of Gomez et al. (Virology 1998, Vol. 249, pages 352-358). Applicant finally points out that Goodman does not address controlling the level of expression with respect to quantity, direction to edible tissues, or

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monocotyledonous plants, as recited in the claims, and points to the instant disclosure of edible plants, tissue specific promoters, monocotyledonous plants, and the use of leader sequences and enhancers. (reply pages 7-9)

The current amendments do not overcome the rejection because they do not clearly distinguish the claimed invention from the teachings of Goodman. With respect to the requirement that the antigen sequence be expressed in “edible” tissue, or that the plant be “edible”, Goodman teaches both expression in edible tissue and edible plants (column 5 lines 51-60). Furthermore, Goodman’s reference to expression in edible tissue and edible plants is not limited to the production of digestive enzymes, but refers specifically to “the mammalian protein product”, which product includes mammalian viral pathogen genes and antigens associated with viral pathogens (column 3 lines 11-13 and 30-36; column 5 lines 51-60). Additionally, the elicitation of an immune response is considered to be a physiologic response, and all of the expressed proteins taught by Goodman are contemplated to be “physiologically active” (column 1 lines 64-67; column 2 lines 10-12).

With respect to the requirement that the antigen be expressed at a level sufficient to induce an immune response when the plant is orally administered to an animal, and the assertion that it was not known in the art at the time of the Goodman reference whether an antigen expressed in a plant consumed by an animal would be digested or be presented to the immune system to allow for recognition, these requirements are desired outcomes of the presence of the nucleotide construct in the claimed transgenic plants. Goodman teaches transgenic plants comprising the same transgenic construct as the claimed transgenic plants. It is not necessary that

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Goodman et al. teach or recognize desired outcomes in order to anticipate the claimed invention, since desired outcomes are inherent properties of the transgenic plants.

Further, with respect the assertion that the levels of expression disclosed in Goodman would not be high enough to achieve an immune response, since Goodman teaches transgenic plants comprising the same transgenic construct as the claimed transgenic plants, the plants taught by Goodman must necessarily have the same expression levels as the claimed transgenic plants, because the plants taught by Goodman would have all the same inherent properties as the claimed transgenic plants.

With respect to the assertion that Applicant's work is peer recognized as the first actual incident of the production of immunogenic viral proteins in plants, the Office notes that it is not necessary that Goodman provide actual working examples of specific embodiments in order to anticipate the claimed invention.

With respect to the assertion that Goodman does not address controlling the level of expression with respect to quantity, such address is not necessary as discussed *supra*. With respect to expression in edible tissues, or monocotyledonous plants, the Office notes that Goodman explicitly addresses these issues at column 4 lines 55-64 and column 5 lines 51-60. Furthermore, Goodman explicitly discloses edible plants, tissue specific promoters, monocotyledonous plants, and the use of leader sequences (column 2 lines 35-45). Explicit reference to enhancers is not required, as claim 73 does not require that all constructs comprise enhancers.

***Remarks***

No claim is allowed.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins

*Cynthia Collins 3/12/04*